that Ca^{2+} influx across the plasma membrane was the only source of LPC Ca^{2+} response in U937 cells. 16:0 and 18:0 LPC induced similar response in Ca^{2+} mobilization. However, 16:0 only induced increase of [^{3}H]thymidine incorporation in this cell line. Recently a couple of G protein-coupled receptors were suggested as LPC receptors. However, our data suggest that LPC-induced responses in monocytes may not be mediated through G protein-coupled receptors and also that other action mechanism of LPC may be involved in the LPC responses, especially cell proliferation, in U937 cells.

[PA1-66] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Direct and functional interaction between dopamine D2 receptor and ALY

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The signaling pathway of D2 dopamine receptor was studied using yeast two-hybrid system. The 3rd cytoplasmic loop of rat D2 dopamine receptor was used to screen the cDNA library of mouse brain, and ALY was found to interact with it. The interaction in the yeast was observed only with the 3rd cytoplasmic loop of D2 dopamine receptor but not with that of D3 or D4 dopamine receptor. The interaction between two proteins was also confirmed by GST pull-down assay. Co-expression of D2 dopamine receptor abolished ALY-induced enhancement of Lef-1 promoter expression in HEK-293 cells. In constrast, when cells were transfected with wnt-1 and dishevelled, ALY and D2 dopamine receptor synergistically enhanced the wnt signaling.

[PA1-67] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Comparative Studies of Molecular Mechanisms of Dopamine D2 and D3 Receptors for the Activation of Extracellular Signal Regulated Kinase 1/2 in HEK-293 cells

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Dopamine D2 and D3 receptors (D2R and D3R) belong to pharmacological D2R family and share similar structural and functional characteristics. Elucidation of their differential functional characteristics is important for understanding their roles in brain. ERK1/2 was chosen as an example of signaling component of D2R and D3R and systemic studies were conducted to understand the regulatory mechanisms on ERK1/2 activation. Agonist-stimulated D2R and D3R induced ERK1/2 activation reached a maximal response at 5 min in a concentration-dependent manner. Haloperidol and sulpiride, antagonists of D2 like receptors, effectively attenuated D2R- and D3R-mediated ERK1/2 activation. Pertussis toxin abolished both D2R- and D3R- mediated ERK1/2 activation, suggesting that either Gi or Go type of G proteins is involved. Dominant negative mutant of dynamin (K44A) blocked ERK activation induced only by D2R but not by D3R. Both D2R and D3R-mediated ERK1/2 activation were attenuated by wortimannin, a inhibitor of phosphatidylinositol 3-kianse, Go6983, a PKC isotype-specific inhibitor. Interestingly, tryphostin AG1478, a selective inhibitor of tyrosine kinase activity in epidermal growth factor receptor and DN-Raf, a dominant negative mutant of p74raf-1 effectively blocked D2R-mediated ERK1/2 activation, but not that mediated by D3R. These results suggest that D2R activates ERK1/2 through the classical ERK1/2 cascades including transactivation with EGFR, however D3R uses distinct signaling pathways for the ERK1/2 activation.

[PA1-68] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]